REMARKS/ARGUMENTS

Reconsideration of this application is requested. Claims 1-3, 6-11, 14 and 15 are in the case.

I. THE 35 U.S.C. §112, SECOND PARAGRAPH, REJECTION

Claims 1-3 and 8-11 and 13-15 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite for the reasons detailed on page 3 of the Action. That rejection is respectfully traversed.

In response, and without conceding to the merit of the rejection, claim 1 has been amended to limit Y^2 to NH_2 and tertiary amino groups wherein the tertiary amino groups are selected from -1-piperazinyl and 4-alkyl-1-piperazinyl. In addition, claim 1 has been amended to recite the dosage range between 500mg/day and 700mg/day. Support appears in claim 13, which has been canceled without prejudice. No new matter is entered. Withdrawal of the outstanding 35 U.S.C. §112, second paragraph, rejection is now respectfully requested.

II. THE ANTICIPATION REJECTIONS

Claims 1-3, 6-9, 11 and 15 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Lunardi *et al.* (Neurology, Vol. 48 (6), 1997, pages 1714-1717, PTO-892) (Lunardi). Claims 1-3, 6-9, 11 and 13 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by WO 00/61231 to Bountra *et al.* (Bountra). Those rejections are respectfully traversed.

The invention as claimed in claim 1 is directed to a method of treating a patient in need of therapy for multiple sclerosis. The method comprises administering to that patient a therapeutically effective dose between 500mg/day and 700mg/day of a compound of formula I wherein R^1, R^2, R^3, R^4 and R^5 are independently selected from hydrogen, trihaloalkyl and halo substituents; X^1, X^2 and X^3 are independently selected from CH, CCH_2F, CCF_3, CO alkyl and CCH_3, and nitrogen atoms, with at two of X^1, X^2 and X^3 being nitrogen, alkyl being preferably ethyl, ethyl or propyl; and Y^1 and Y^2 are independently selected from hydrogen, NH_2 and tertiary amino groups wherein the tertiary amino groups are selected from -1-piperazinyl and 4-alkyl-1-piperazinyl.

Applicant does not agree with the assertion in the Action that Lunardi teaches treating multiple sclerosis sufferers with 400mg/day. However, in order to advance prosecution, and without conceding to the rejection, the minimum claimed dose has been amended to 500mg/day. Based on this, it is clear that Lunardi does not constitute an anticipatory disclosure, inherently or otherwise, of the presently claimed treatment. Withdrawal of the anticipation rejection based on Lunardi is respectfully requested.

Bountra likewise contains no disclosure of the method as claimed. Bountra proposes that sodium channel antagonists may be used to treat neuronal apoptosis. This is irrelevant to multiple sclerosis (MS), as it is well evidenced in the art that this mechanism is not significant in that disease. Moreover, Bountra contains no disclosure of the claimed range of 500mg/day and 700mg/day.

Applicant reiterates its observations that the role of apoptosis in the aetiology of MS appears equivocal and unproven, as particularly illustrated by the disclosure of G

Ramsaransing et al: B Med Journal p1113 (22nd April 2000) that use of the sodium channel blocker carbamazepine **makes multiple sclerosis worse**.

The Cannella *et al.*, Goertsches *et al.* and Singh *et al.* papers referred to in the prior response of April 2, 2008 are again referred to in support of Applicant's position. The scientific argument presented in Bountra's Summary of Invention and Claims for the use of compounds which inhibit apoptosis in the treatment of relapse and EDSS in MS appears unfounded and not credible. Furthermore, Smith and Meldrum, 1995 (Cerebral protective effect of lamotrigine after focal ischemia in rats, Stroke:26,117-122) showed that lamotrigine is only neuroprotective in models of focal ischemia over a narrow dose range. In fact, only a dose of 20mg/kg significantly reduced neurological scores. Based on this, and the papers cited above, one of ordinary skill in the art would not have a reasonable expectation that the presently claimed dose would be efficacious as now disclosed.

It is clear that the invention as claimed is not anticipated by Lunardi or Bountra. Reconsideration and withdrawal of the outstanding anticipation rejections are accordingly respectfully requested.

III. THE OBVIOUSNESS REJECTION

Claims 10, 14 and 15 stand rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Bountra. That rejection is respectfully traversed.

For the reasons outlined above, Bountra does not render the present invention obvious. Bountra contains no suggestion of the claimed range of 500mg/day and 700mg/day, and provides no credible guidance on how to dose and what to dose. A

person of ordinary skill in the art might easily have selected carbamazepine, as did Ramsaransing *et al*, and then dose at 900mg with serious detrimental effect.

The present invention meets the requirements of patentability in so far as it provides a significantly improved treatment of a seriously debilitating disease. The current gold standard medicaments Copaxone and interferon are surpassed in effectiveness by the surprising selection of a previously undisclosed selected high dose of a medicament previously administered for pain control but otherwise predictable by comparison with medicines of similar action to be likely to make the disease worse.

For the reasons detailed above, one of ordinary skill would not have been motivated to arrive at the invention as now claimed based on Bountra. Absent any such motivation, a *prima facie* case of obviousness has not been generated in this case. Reconsideration and withdrawal of the outstanding obviousness rejection are accordingly respectfully requested.

Favorable action on this application is awaited.

Respectfully submitted,

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